

What is claimed is:

1. An assay method comprising:

(A) generating:

1) at least a first fragment of a reporter molecule linked to a first interacting domain and at least a second fragment of a reporter molecule linked to a second interacting domain, or

2) nucleic acid molecules that code for A)1) and subsequently allowing said nucleic acid molecules to produce their coded products; then,

(B) allowing interaction of said domains; and

(C) detecting reconstituted reporter molecule activity,

where said reporter molecule can react with a penicillin- or cephalosporin-class substrate.

2. An assay according to Claim 1 where said reporter molecule is an enzyme.

3. An assay according to Claim 1 where said reporter molecule is a  $\beta$ -lactamase.

4. An assay according to Claim 1 where said reaction with said substrate is essentially irreversible.

5. An assay according to Claim 1, 2, 3, or 4 where said substrate comprises Nitrocefin or CCF2/AM.

6. An assay according to Claim 1, 2, 3, or 4 performed *in vivo*.



1) at least a first fragment of a reporter molecule linked to a first interacting domain and at least a second fragment of a reporter molecule linked to a second interacting domain; or

2) compounds that code therefor; and

(B) detecting reconstituted reporter molecule activity, where a reporter molecule substrate is added that becomes trapped within said cell after entrance therein.

13. An assay method comprising:

(A) exposing a host cell to:

1) at least a first fragment of a reporter molecule linked to a first interacting domain and at least a second fragment of a reporter molecule linked to a second interacting domain; or

2) compounds that code therefor; and

(B) detecting reconstituted reporter molecule activity, where a reporter molecule substrate is added that has a fluorescent signal-producing system covalently associated therewith.

14. An assay according to Claim 13 wherein cleavage of said substrate by said reporter molecule results in a change in fluorescent signal production.

15. An assay according to Claim 1, 7, 8, 12, or 13 where a compound is added that leads to a detectable decrease in reporter molecule activity by decreasing interaction between interacting domains.

16. An assay method comprising:

(A) exposing a host cell to:

1) at least a first fragment of a reporter molecule linked to a first interacting domain and at least a second fragment of a reporter molecule linked to a second interacting domain; or

2) compounds that code therefor; and

(B) detecting host cell survival as an indication of reconstituted reporter molecule activity.

17. An assay method comprising:

(A) exposing a host cell to:

1) at least a first fragment of a reporter molecule linked to a first interacting domain and at least a second fragment of a reporter molecule linked to a second interacting domain; or

2) compounds that code therefor;

(B) further exposing said cell to a compound to be assayed for its ability to interfere with interaction of said first and second domains; and

(C) detecting host cell survival as an indication of interference with said interaction.

18. A composition comprising a compound which comprises a fragment of an interacting domain linked to a fragment of a reporter molecule that can hydrolyze either a penicillin class substrate or a cephalosporin class substrate.

19. A composition comprising:

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(A) a first compound comprising a first fragment of an interacting domain linked to a first fragment of a reporter molecule that can hydrolyze either a penicillin class substrate or a cephalosporin class substrate; and

(B) a second compound comprising a second fragment of an interacting domain linked to a second fragment said reporter molecule.

20. A composition according to Claim 18 or 19 where said reporter molecule is an enzyme.

21. A composition according to Claim 18 or 19 where said reporter molecule is a  $\beta$ -lactamase.

22. A composition according to Claim 18 or 19 where said interacting domain is derived from a leucine zipper or from a rapamycin-inducible interacting protein.

23. A composition according to Claim 18 or 19 where said interacting domain is derived from a GCN 4 leucine zipper or from FKBP/FRB.

24. A composition according to Claim 18 or 19 wherein at least one of said compounds has a flexible linker joining its reporter molecule fragment to its associated interacting domain.

25. A nucleic acid molecule comprising a sequence that codes for any of the compounds according to Claim 18 or 19.

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26. A nucleic acid molecule comprising a sequence that codes for any of the compounds according to Claim 20.

27. A nucleic acid molecule comprising a sequence that codes for any of the compounds according to Claim 21.

28. A nucleic acid molecule comprising a sequence that codes for any of the compounds according to Claim 22.

29. A nucleic acid molecule comprising a sequence that codes for any of the compounds according to Claim 23.

30. A nucleic acid molecule comprising a sequence that codes for any of the compounds according to Claim 24.

31. A vector comprising any of the nucleic acids according to Claim 25.

32. A vector comprising any of the nucleic acids according to Claim 26.

33. A vector comprising any of the nucleic acids according to Claim 27.

34. A vector comprising any of the nucleic acids according to Claim 28.

35. A vector comprising any of the nucleic acids according to Claim 29.

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36. A vector comprising any of the nucleic acids according to Claim 30.

37. A cell in contact with any of the compounds according to Claim 18 or 19 or with any molecule that codes for any of said compounds.

38. A cell in contact with any of the compounds according to Claim 20 or with any molecule that codes for any of said compounds.

39. A cell in contact with any of the compounds according to Claim 21 or with any molecule that codes for any of said compounds.

40. A cell in contact with any of the compounds according to Claim 22 or with any molecule that codes for any of said compounds.

41. A cell in contact with any of the compounds according to Claim 23 or with any molecule that codes for any of said compounds.

42. A cell in contact with any of the compounds according to Claim 24 or with any molecule that codes for any of said compounds.

43. An assay method comprising:

(A) allowing at least two molecules capable of mutual interaction to draw into close molecular proximity at least two reporter molecule fragments which, when in close molecular

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proximity, form a complex capable of reaction with a penicillin- or cephalosporin-class substrate;  
and

(B) detecting a signal resulting from said reaction.

44. An assay according to Claim 43 where said reporter molecule is an enzyme.

45. An assay according to Claim 43 where said reporter molecule is a  $\beta$ -lactamase.

46. An assay according to Claim 43 where said reaction with said substrate is essentially irreversible.

47. An assay according to Claims 43, 44, 45, or 46 where said substrate comprises Nitrocefin or CCF2/AM.

48. An assay according to Claims 43, 44, 45, or 46 performed *in vivo*.

49. An assay according to Claims 43, 44, 45, or 46 where said reporter molecule is not normally present in eukaryotes.

50. An assay according to Claims 43, 44, 45, or 46 where there is essentially no intrinsic background in the assay.

51. An assay method comprising:

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(A) allowing at least two molecules capable of mutual interaction to draw into close molecular proximity at least two reporter molecule fragments which, when in close molecular proximity, form a complex capable of reaction with a penicillin- or cephalosporin-class substrate; and

(B) detecting a signal resulting from said reaction, where there is essentially no intrinsic background in the assay.

52. An assay according to Claims 43, 44, 45, or 46, or 51 whose signal to background ratio is about 30:1 or higher. ✓

53. An assay according to Claims 43, 44, 45, or 46, or 51 where said signal can be observed by eye. ✓

54. An assay according to Claim 53 where said substrate comprises Nitrocefin.

55. An assay according to Claims 43, 44, 45, or 46, or 51 where said reaction occurs with a cell and said substrate becomes trapped within said cell after entrance therein.

56. An assay method comprising:

(A) allowing at least two molecules capable of mutual interaction to draw into close molecular proximity at least two reporter molecule fragments which, when in close molecular proximity, form a complex capable of reaction with a penicillin- or cephalosporin-class substrate; and

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(B) detecting a signal resulting from said reaction, where said reaction occurs with a cell and said substrate becomes trapped within said cell after entrance therein.

57. An assay according to Claims 43, 44, 45, or 46, or 51 where a reporter molecule substrate is added that has a fluorescent signal-producing system covalently associated therewith.

58. An assay method comprising:

(A) allowing at least two molecules capable of mutual interaction to draw into close molecular proximity at least two reporter molecule fragments which, when in close molecular proximity, form a complex capable of reaction with a penicillin- or cephalosporin-class substrate; and

(B) detecting a signal resulting from said reaction, where a reporter molecule substrate is added that has a fluorescent signal-producing system covalently associated therewith.

59. An assay according to Claim 58 where said reaction results in a change in fluorescent signal production.

60. An assay according to Claim 58 where a compound is added that leads to a detectable decrease in reporter molecule activity by interfering with said mutual interaction.

61. A cellular assay method comprising:

(A) allowing at least two molecules capable of mutual interaction to draw into close molecular proximity at least two reporter molecule fragments which, when in close molecular

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proximity, form a complex capable of reaction with a penicillin- or cephalosporin-class substrate;  
and

(B) detecting cell survival as an indication of said reaction.

62. An assay according to Claim 61 where a compound capable of interfering with said mutual interaction is added.

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